

SEQUENCE LISTING

<110> Hisamitsu Pharmaceutical Co., Inc.

<120> METHOD OF SCREENING COMPOUND CAPABLE OF ACCELERATING OR INHIBITING APOPTOSIS, APOPTOSIS ACCELERATOR AND APOPTOSIS INHIBITOR

<130> FP05-0112-00

<150> JP 2004-93, 266

<151> 2004-03-26

<150> JP 2004-176, 107

<151> 2004-06-14

<160> 26

<170> PatentIn version 3.1

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Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr
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Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu
 35 40 45

Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
 50 55 60

Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
 65 70 75 80

Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
 85 90 95

Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
 100 105 110

Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
 115 120 125

Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
 130 135 140

Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
145 150 155 160

His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
165 170 175

Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
180 185 190

Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
195 200 205

Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
210 215 220

Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
225 230 235 240

Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
245 250 255

His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
260 265 270

Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
275 280 285

Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
290 295 300

Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
305 310 315 320

Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
325 330 335

Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
340 345 350

Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
355 360 365

Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
370 375 380

Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
385 390 395 400

Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
405 410 415

Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
420 425 430

Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln

435

440

445

Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
450 455 460

Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
465 470 475 480

Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
485 490 495

Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
500 505 510

Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
515 520 525

Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Glu Leu
530 535 540

Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu
545 550 555 560

Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser
565 570 575

Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His
580 585 590

Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu
595 600 605

Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
610 615 620

Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
625 630 635 640

Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
645 650 655

Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
660 665 670

Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
675 680 685

Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu
690 695 700

Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu
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Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met
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Asn Leu Asp Trp Ser Trp Leu Thr Glu
740 745

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<223> IKK-alpha (K44A)

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20 25 30

Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Ala Ser Cys Arg Leu
35 40 45

Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
50 55 60

Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
65 70 75 80

Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
85 90 95

Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
100 105 110

Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
115 120 125

Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
130 135 140

Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
145 150 155 160

His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
165 170 175

Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
180 185 190

Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
195 200 205

Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
210 215 220

Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
225 230 235 240

Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser

245

250

255

His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
 260 265 270

Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
 275 280 285

Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
 290 295 300

Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
 305 310 315 320

Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
 325 330 335

Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
 340 345 350

Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
 355 360 365

Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
 370 375 380

Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
 385 390 395 400

Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
 405 410 415

Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
 420 425 430

Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln
 435 440 445

Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
 450 455 460

Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
 465 470 475 480

Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
 485 490 495

Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
 500 505 510

Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
 515 520 525

Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Glu Leu
 530 535 540

Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu

545 550 555

Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser

565 570 575

Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His

580 585 590

Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu

595 600 605

Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys

610 615 620

Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met

625 630 635 640

Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile

645 650 655

Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu

660 665 670

Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala

675 680 685

Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu

690 695 700

Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu

705 710 715 720

Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met

725 730 735

Asn Leu Asp Trp Ser Trp Leu Thr Glu

740 745

<210> 26

<211> 1173

<212> PRT

<213> Homo sapiens

<400> 26

Met Glu Glu Leu Ser Ala Asp Glu Ile Arg Arg Arg Arg Leu Ala Arg

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Leu Ala Gly Gly Gln Thr Ser Gln Pro Thr Thr Pro Leu Thr Ser Pro

20 25 30

Gln Arg Glu Asn Pro Pro Gly Pro Pro Ile Ala Ala Ser Ala Pro Gly

35 40 45

Pro Ser Gln Ser Leu Gly Leu Asn Val His Asn Met Thr Pro Ala Thr

50 55 60

Ser Pro Ile Gly Ala Ser Gly Val Ala His Arg Ser Gln Ser Ser Glu

65 70 75 80

Gly Val Ser Ser Leu Ser Ser Ser Pro Ser Asn Ser Leu Glu Thr Gln

85 90 95

Ser Gln Ser Leu Ser Arg Ser Gln Ser Met Asp Ile Asp Gly Val Ser

100 105 110

Cys Glu Lys Ser Met Ser Gln Val Asp Val Asp Ser Gly Ile Glu Asn

115 120 125

Met Glu Val Asp Glu Asn Asp Arg Arg Glu Lys Arg Ser Leu Ser Asp

130 135 140

Lys Glu Pro Ser Ser Gly Pro Glu Val Ser Glu Glu Gln Ala Leu Gln

145 150 155 160

Leu Val Cys Lys Ile Phe Arg Val Ser Trp Lys Asp Arg Asp Arg Asp

165 170 175

Val Ile Phe Leu Ser Ser Leu Ser Ala Gln Phe Lys Gln Asn Pro Lys

180 185 190

Glu Val Phe Ser Asp Phe Lys Asp Leu Ile Gly Gln Ile Leu Met Glu

195 200 205

Val Leu Met Met Ser Thr Gln Thr Arg Asp Glu Asn Pro Phe Ala Ser

210 215 220

Leu Thr Ala Thr Ser Gln Pro Ile Ala Ala Ala Ala Arg Ser Pro Asp

225 230 235 240

Arg Asn Leu Leu Leu Asn Thr Gly Ser Asn Pro Gly Thr Ser Pro Met

245 250 255

Phe Cys Ser Val Ala Ser Phe Gly Ala Ser Ser Leu Ser Ser Leu Gly

260 265 270

Ala Ser Gly Gly Ala Ser Asn Trp Asp Ser Tyr Ser Asp His Phe Thr

275 280 285

Ile Glu Thr Cys Lys Glu Thr Asp Met Leu Asn Tyr Leu Ile Glu Cys

290 295 300

Phe Asp Arg Val Gly Ile Glu Glu Lys Lys Ala Pro Lys Met Cys Ser

305 310 315 320

Gln Pro Ala Val Ser Gln Leu Leu Ser Asn Ile Arg Ser Gln Cys Ile

325 330 335

Ser His Thr Ala Leu Val Leu Gln Gly Ser Leu Thr Gln Pro Arg Ser

340 345 350

Leu Gln Gln Pro Ser Phe Leu Val Pro Tyr Met Leu Cys Arg Asn Leu

355 360 365

Pro Tyr Gly Phe Ile Gln Glu Leu Val Arg Thr Thr His Gln Asp Glu
370 375 380

Glu Val Phe Lys Gln Ile Phe Pro Ile Leu Gln Gly Leu Ala Leu
385 390 395 400

Ala Ala Lys Glu Cys Ser Leu Asp Ser Asp Tyr Phe Lys Tyr Pro Leu
405 410 415

Met Ala Leu Gly Glu Leu Cys Glu Thr Lys Phe Gly Lys Thr His Pro
420 425 430

Val Cys Asn Leu Val Ala Ser Leu Arg Leu Trp Leu Pro Lys Ser Leu
435 440 445

Ser Pro Gly Cys Gly Arg Glu Leu Gln Arg Leu Ser Tyr Leu Gly Ala
450 455 460

Phe Phe Ser Phe Ser Val Phe Ala Glu Asp Asp Val Lys Val Val Glu
465 470 475 480

Lys Tyr Phe Ser Gly Pro Ala Ile Thr Leu Glu Asn Thr Arg Val Val
485 490 495

Ser Gln Ser Leu Gln His Tyr Leu Glu Leu Gly Arg Gln Glu Leu Phe
500 505 510

Lys Ile Leu His Ser Ile Leu Leu Asn Gly Glu Thr Arg Glu Ala Ala
515 520 525

Leu Ser Tyr Met Ala Ala Val Val Asn Ala Asn Met Lys Lys Ala Gln
530 535 540

Met Gln Thr Asp Asp Arg Leu Val Ser Thr Asp Gly Phe Met Leu Asn
545 550 555 560

Phe Leu Trp Val Leu Gln Gln Leu Ser Thr Lys Ile Lys Leu Glu Thr
565 570 575

Val Asp Pro Thr Tyr Ile Phe His Pro Arg Cys Arg Ile Thr Leu Pro
580 585 590

Asn Asp Glu Thr Arg Val Asn Ala Thr Met Glu Asp Val Asn Asp Trp
595 600 605

Leu Thr Glu Leu Tyr Gly Asp Gln Pro Pro Phe Ser Glu Pro Lys Phe
610 615 620

Pro Thr Glu Cys Phe Phe Leu Thr Leu His Ala His His Leu Ser Ile
625 630 635 640

Leu Pro Ser Cys Arg Arg Tyr Ile Arg Arg Leu Arg Ala Ile Arg Glu
645 650 655

Leu Asn Arg Thr Val Glu Asp Leu Lys Asn Asn Glu Ser Gln Trp Lys
660 665 670

Asp Ser Pro Leu Ala Thr Arg His Arg Glu Met Leu Lys Arg Cys Lys
675 680 685

Thr Gin Leu Lys Lys Leu Val Arg Cys Lys Ala Cys Ala Asp Ala Gly
690 695 700

Leu Leu Asp Glu Ser Phe Leu Arg Arg Cys Leu Asn Phe Tyr Gly Leu
705 710 715 720

Leu Ile Gin Leu Leu Leu Arg Ile Leu Asp Pro Ala Tyr Pro Asp Ile
725 730 735

Thr Leu Pro Leu Asn Ser Asp Val Pro Lys Val Phe Ala Ala Leu Pro
740 745 750

Glu Phe Tyr Val Glu Asp Val Ala Glu Phe Leu Phe Phe Ile Val Gin
755 760 765

Tyr Ser Pro Gin Ala Leu Tyr Glu Pro Cys Thr Gin Asp Ile Val Met
770 775 780

Phe Leu Val Val Met Leu Cys Asn Gin Asn Tyr Ile Arg Asn Pro Tyr
785 790 795 800

Leu Val Ala Lys Leu Val Glu Val Met Phe Met Thr Asn Pro Ala Val
805 810 815

Gln Pro Arg Thr Gin Lys Phe Phe Glu Met Ile Glu Asn His Pro Leu
820 825 830

Ser Thr Lys Leu Leu Val Pro Ser Leu Met Lys Phe Tyr Thr Asp Val
835 840 845

Glu His Thr Gly Ala Thr Ser Glu Phe Tyr Asp Lys Phe Thr Ile Arg
850 855 860

Tyr His Ile Ser Thr Ile Phe Lys Ser Leu Trp Gin Asn Ile Ala His
865 870 875 880

His Gly Thr Phe Met Glu Glu Phe Asn Ser Gly Lys Gin Phe Val Arg
885 890 895

Tyr Ile Asn Met Leu Ile Asn Asp Thr Thr Phe Leu Leu Asp Glu Ser
900 905 910

Leu Glu Ser Leu Lys Arg Ile His Glu Val Gin Glu Glu Met Lys Asn
915 920 925

Lys Glu Gin Trp Asp Gin Leu Pro Arg Asp Gin Gin Ala Arg Gin
930 935 940

Ser Gin Leu Ala Gin Asp Glu Arg Val Ser Arg Ser Tyr Leu Ala Leu
945 950 955 960

Ala Thr Glu Thr Val Asp Met Phe His Ile Leu Thr Lys Gin Val Gin

965

970

975

Lys Pro Phe Leu Arg Pro Glu Leu Gly Pro Arg Leu Ala Ala Met Leu
980 985 990

Asn Phe Asn Leu Gln Gln Leu Cys Gly Pro Lys Cys Arg Asp Leu Lys
995 1000 1005

Val Glu Asn Pro Glu Lys Tyr Gly Phe Glu Pro Lys Lys Leu Leu
1010 1015 1020

Asp Gln Leu Thr Asp Ile Tyr Leu Gln Leu Asp Cys Ala Arg Phe
1025 1030 1035

Ala Lys Ala Ile Ala Asp Asp Gln Arg Ser Tyr Ser Lys Glu Leu
1040 1045 1050

Phe Glu Glu Val Ile Ser Lys Met Arg Lys Ala Gly Ile Lys Ser
1055 1060 1065

Thr Ile Ala Ile Glu Lys Phe Lys Leu Leu Ala Glu Lys Val Glu
1070 1075 1080

Glu Ile Val Ala Lys Asn Ala Arg Ala Glu Ile Asp Tyr Ser Asp
1085 1090 1095

Ala Pro Asp Glu Phe Arg Asp Pro Leu Met Asp Thr Leu Met Thr
1100 1105 1110

Asp Pro Val Arg Leu Pro Ser Gly Thr Ile Met Asp Arg Ser Ile
1115 1120 1125

Ile Leu Arg His Leu Leu Asn Ser Pro Thr Asp Pro Phe Asn Arg
1130 1135 1140

Gln Thr Leu Thr Glu Ser Met Leu Glu Pro Val Pro Glu Leu Lys
1145 1150 1155

Glu Gln Ile Gln Ala Trp Met Arg Glu Lys Gln Asn Ser Asp His
1160 1165 1170